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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Flehr Hohbach Test
Albritton & Herbert
Suite 3400
Four Embarcadero Center
San Francisco, CA 94111

EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	7

DATE MAILED: 06/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,525	MCKEOWN ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5 and 10-12* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The response filed on September 23, 2002 (Paper No. 6) to the restriction requirement of July 2, 2002 has been received. Applicant has elected Group II, claims 2-5 and 10-12 for examination with traverse. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a).

Claims 1, and 6-9 have been cancelled by Applicant's amendment in Paper No. 6.

Claims 2-5, and 10-12 are currently pending and are under consideration. It is noted, however, that claim 11, objected to below, and has not been further treated on the merits because said claim is multiple dependent claim that is dependent on multiple dependent claims.

Claim Objections

Claim 11 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim 4 is objected to for reciting "available from Oncogene Science, Inc." as such language is improper claim terminology.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5 and 12 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a correlation step describing how the results of the method relate back to the preamble of the method objectives including comparison to normal or controlled individual.

Claims 5 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claims 5 and 12 provide for the use of antibodies to the 37 Kda fragment of EGFR, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-3 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the diagnosis of first presentation or recurrence of bladder cancer,or a method for diagnosing a urinary infection consisting of detecting a 37kDa fragment of epidermal growth factor receptor (EGFR) in a urine sample wherein the presence of the fragment is detected using antibody Ab4, does not reasonably provide enablement for the method as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the

predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to diagnosing the presence or recurrence of bladder cancer or the diagnosis of prostate cancer or the diagnosis of a urinary infection comprising or consisting of testing for the presence of a 37 kDa fragment of EGFR in a urine sample.

The specification teaches (page 5, lines 15+) that a 37 kDa EGFR fragment has been detected in urine with bladder patients wherein samples were probed with the Ab4 antibody which appears to recognize an internal domain of the receptor via Western blot analysis. The specification further teaches (page 6, Experiment 2) that the 37 kDA EGFR fragment was also detected in patients with urinary infection and prostate cancer.

However, one cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to diagnosing bladder cancer by detecting the 37 kDa fragment of EGFR in urine by using any all antibodies (Claim 3) or by any other mode of detection (Claims 2 and 10) and applicant has not enabled all of these types of modified assays because it has not been shown that the *same* 37 kDA fragment can be consistently detected by any other antibodies other than the Ab4 antibody. And, although the specification teaches (page 11, line 12) that other antibodies can be developed which are specific to the 37 kDA fragment, applicants have not taught how one of ordinary skill in the art would be able to produce antibodies which would predictably and specifically recognize an epitope of EGFR that would immunoprecipitate the same 37kDa fragment as applicants with the same diagnostic qualities. Hence, there is insufficient guidance and direction to one of skill in the art to predictably diagnose bladder cancer (or a urinary infection) by any and all means including all antibodies

that may or may not immunoprecipitate a diagnostic fragment of EGFR that is 37 kDa. Furthermore, applicants are not enabled to the scope of the claims drawn to diagnosing "prostate" cancer comprising a test for the presence of a 37 kDa fragment of EGFR in a urine sample as the specification teaches that of 10 prostate cancer samples, 5 had the 37 kDa fragment and 5 did not have the 37 kDa fragment. At best, the results are ambiguous because they do not teach one of skill in the art that prostate cancer can be reliably diagnosed in a predictable manner solely by detecting the presence of the 37 kDa fragment. In fact, the specification teaches (page 7, line 11) that the inclusion of prostate cancer patients could be a confounding factor as only 50% of the samples were positive. Hence, one of ordinary skill in the art would not know how to use the invention as broadly claimed since there is a 50% chance that the test would not reliably identify the presence of prostate cancer.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to predictably practice the claimed invention as broadly claimed. Thus, only a method for the diagnosis of first presentation or recurrence of bladder cancer (or urinary infection) consisting of the detection of a 37 kDa fragment of EGFR in a urine sample wherein the presence of the 37 kDA EGFR fragment is detected using the Ab4 antibody is enabled. Therefore, undue experimentation would be required to enable the claims as written.

Claims **4-5** are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are (1)

known and readily available to the public; (2) reproducible from a written description (e.g. sequenced); or (3) deposited.

The claims are drawn to the use of an antibody **Ab4**. It is noted however that the specification does not appear to teach whether the Ab4 antibody is a monoclonal or polyclonal species. Thus, it is assumed, for examination purposes, that the Ab4 antibody is a monoclonal antibody.

The specification teaches (page 11, lines 5-6) that the Ab-4 antibody is available from Oncogene Science, Inc. as catalogue No. HCS16.

MPEP 2404 states that biological material need not be deposited, inter alia, if it is known and readily available to the public or can be made or isolated without undue experimentation. However, it is unclear if a cell line which produces an antibody having the exact structural and chemical identity of monoclonal antibodies selected from the group consisting of **Ab4,** are known and publicly available, or can be reproducibly isolated without undue experimentation. Clearly, without access to the hybridoma cell lines producing said monoclonal antibodies, it would not be possible to practice the claimed invention. Secondly, at the time of this examination, the PTO could not establish whether or not the AB4 antibody was commercially available from Oncogene Science Inc. MPEP 2401.1 further states that in an application where the invention requires access to specific biological material, applicant could show that the biological material is accessible because it is known and readily available to the public. The concepts of "known and readily available" are considered to reflect a level of public accessibility to a necessary component of an invention disclosure that is consistent with an ability to make and

use the invention. To avoid the need for a deposit on this basis, the biological material must be **both known and readily available** - neither concept alone is sufficient.

Thus, to obviate this rejection applicant must provide an affidavit or declaration swearing that the Ab4 antibody is commercially available because without such assurance, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 10, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Ritchie *et al.* BRITISH JOURNAL OF CANCER, (MAY 1998) Vol. 78, Supp. [1], Abstract No. P118, page 54.

The claims are broadly drawn to a method for the diagnosis of bladder cancer, and/or prostate cancer and/or urinary infection, the method comprising a test for the presence of a 37Kda fragment of EGFR in a urine sample. The claims are further drawn to the generic use of the Ab4 antibody for detecting bladder cancer.

Ritchie *et al.* teach a method for the diagnosis of bladder cancer, the method "comprising" a test for EGFR in a urine sample. Although Ritchie *et al.* do not specifically teach that a 37Kda fragment of EGFR was detected, the reference teaches that the tumor tissue was visualized using the Ab4 antibody against EGFR. Thus, since the specification teaches that the

Ab4 antibody will detect a 37kDa fragment of EGFR, the prior art's usage of the Ab4 antibody in a method comprising a test for the presence of the a 37kDa fragment of EGFR inherently anticipates the claims. It is noted that Claim 2 is NOT anticipated by the reference because claim 2 is solely drawn to a method "consisting" of the detection of the 37kDa fragment.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
June 23, 2003

Gary B. Nickol